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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,815	06/08/2001	Takashi Ito	46342/55965	9695

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EDWARDS & ANGELL, LLP
P.O. BOX 9169
BOSTON, MA 02209

EXAMINER

DEBERRY, REGINA M

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 05/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/857,815	Applicant(s) ITO ET AL.	
	Examiner Regina M. DeBerry	Art Unit 1647	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 10 October 2002.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-16 is/are pending in the application.

4a) Of the above claim(s) 14 and 16 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-13 and 15 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claim(s) 1-16 are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☒ All b) ☐ Some * c) ☐ None of:
 1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> .	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input type="checkbox"/> Other: _____
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Status of Application, Amendments and/or Claims

The information disclosure statement filed 08 June 2001 (Paper No. 3) was received.

The amendment filed 28 September 2001 (Paper No. 4) has been entered in full. Applicant's election with traverse of Group I (claims 1-13, 15 and SEQ ID NO:38) in Paper No. 13 (10 October 2002) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 14 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 13. Claims 1-13, 15 and SEQ ID NO:38 are under examination.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy (Japan 10/350377 and Japan 11/55326) and the verified English language translation of each document have been filed in parent Application No. 09/857815, filed on 29 March 2002 (Paper No. 10).

Sequence Rules

The specification is not in compliance with 37 CFR 1.821-1.825 of the Sequence Rules and Regulations. When the description of a patent application discusses a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of the Sequence Rules and Regulations, reference must be made to the sequence

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by use of the assigned identifier (SEQ ID NO:), in the text and claims of the patent application. The specification refers to sequences in Figure 10 and on page 11 (lines 7-12) but does not identify the sequences by their sequence identifiers.

Sequences appearing in drawings may be referenced in the drawings themselves or in the corresponding Brief Description thereof. **Appropriate correction is required.**

Applicant must submit a response to this Office Action and compliance with sequence rules simultaneously.

Claim Objections

Claims 2, 5-7, 10 and 11 are objected to because of the following informalities:

Claim 2 is objected to because of the spelling of "ratioof".

Claims 5-7, 10 and 11 encompass non-elected inventions (SEQ ID Nos) and require amendment to limit to elected invention. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13, 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

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one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant claims are drawn to a betacellulin mutein or a salt thereof, wherein the pancreatic β cell differentiation promoting activity is preserved, and the epithelial cell growth promoting activity is reduced, a betacellulin mutein or salt thereof according to claim 1, wherein the ratio of the pancreatic β cell differentiation promoting activity to the epithelial cell growth promoting activity is at least twice relative to that of betacellulin, and a method for prophylaxis or treatment for diabetes characterized in that betacellulin mutein or salt thereof according to claim 1 is administered to mammals.

The specification teaches the construction and purification of BTC24-76 (SEQ ID NO:38) (specification, Examples 16-18). The results of the EGF binding assay and β cell differentiation promoting activity for BTC24-76 (SEQ ID NO:38) were summarized in Table 14 (specification, page 101). The subject matter sought to be patented as defined by the claims is not supported by an enabling disclosure because the specification fails to teach how to make a betacellulin mutein (SEQ ID NO:38) wherein the β cell differentiation promoting activity is preserved and the epithelial growth promoting activity is reduced and wherein the ratio of the pancreatic β cell differentiation promoting activity to the epithelial cell growth promoting activity is at least twice relative to that of betacellulin. The results of BTC24-76 (SEQ ID NO:38) presented in Table 14 do not concur with the limitations of the claims.

In addition, the specification fails to teach how to use BTC24-76 in a method for the prophylaxis or treatment for diabetes in mammals. The specification fails to disclose

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a direct correlation (working examples, animal models, etc.) between the use of the instant invention and treatment in subjects for diabetes. Further, claim 15 recites the limitation prophylaxis. Prophylaxis means to completely stop a condition from occurring. "Prophylaxis" is not a relative term, it is total. This would require administration of the claimed formulations prior to the development of diabetes. However, there is no guidance in the specification for determining the appropriate time prior to the development of diabetes to begin the therapy or for identifying patients at risk for developing diabetes. A very high degree of evidence is required, which is accepted in the art, that an absolute protection from the pathology exists over an extended period of time. The specification provides insufficient guidance with regard to the issues raised above and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed methods with a reasonable expectation of success. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention. The specification is not enabled for a method for prophylaxis or treatment for diabetes, characterized in that a betacellulin mutein or salt thereof according to claim 1 is administered to mammals.

Due to the large quantity of experimentation necessary to show a correlation between a betacellulin mutein or salt thereof according to claim 1 and prophylaxis or treatment of diabetes in mammals, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite

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limitations regarding amounts/routes of administration and parameters for the prevention of diabetes, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-5, 8 and 9 are indefinite because they recite alterations of specifically numbered amino acid residues without reciting a reference sequence (SEQ ID NO:).

Claims 5-7, 10 and 11 are indefinite in the recitation "an amino acid sequence *represented by* SEQ ID NO:". It is not clear if the claims read on "open" or "closed" language.

The metes and bounds of the instant claims cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

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The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 3 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Wei *et al.*, US Patent No. 6,410,506 B1. Claim 7 is drawn to a betacellulin mutein or salt thereof according to claim 3, comprising (1) an amino acid sequence represented by SEQ ID NO:37, or (2) an amino acid sequence represented by SEQ ID NO:38. Wei *et al.* teach an amino acid sequence comprising the sequence represented by SEQ ID NO:38. Claim 7 encompasses all of the limitations of claims 1 and 3. Please see Wei *et al.*, SEQ ID NO:13.

Conclusion

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on Mondays-Fridays 8:00 a.m. - 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



RMD
May 16, 2003



GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600